```
=> fil medl; d que l14; fil wpids; d que l23; fil biosis; d que l31
FILE 'MEDLINE' ENTERED AT 09:58:10 ON 04 JAN 96

 FILE LAST UPDATED: 27 DEC 1995 (951227/UP). FILE COVERS 1966 TO DATE.
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 MEDLINE, CANCERLIT AND PDQ ERRONEOUSLY ANNOTATED CERTAIN ARTICLES
 AUTHORED OR CO-AUTHORED BY DR. BERNARD FISHER WITH THE PHRASE
 "SCIENTIFIC MISCONDUCT-DATA TO BE REANALYZED." ALL SUCH ANNOTATIONS
 HAVE BEEN REMOVED OR ARE BEING REMOVED. WE APOLOGIZE FOR ANY PROBLEMS
 OR CONCERNS THIS MAY HAVE CAUSED. USERS SHOULD DISREGARD THOSE PRIOR
 ANNOTATIONS.


L1          9702 SEA FILE=MEDLINE SOMATOMEDINS+NT/CT
L2        187529 SEA FILE=MEDLINE ISCHEMIA+NT/CT
L4         16386 SEA FILE=MEDLINE KIDNEY FAILURE, ACUTE+NT/CT
L7          2634 SEA FILE=MEDLINE L1(L)(TU OR PD)
L12       139899 SEA FILE=MEDLINE L2/MAJ
L13        11030 SEA FILE=MEDLINE L4/MAJ
L14           17 SEA FILE=MEDLINE L7 AND (L12 OR L13)


FILE 'WPIDS' ENTERED AT 09:58:11 ON 04 JAN 96
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FILE LAST UPDATED: 21 DEC 95                  <951221/UP>
>>>UPDATE WEEKS:
MOST RECENT DERWENT WEEK              9551    <199551/DW>
DERWENT WEEK FOR CHEMICAL CODING:     9539
DERWENT WEEK FOR POLYMER INDEXING:    9546
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
>>> DERWENT POLYMER INDEXING THESAURUS AVAILABLE IN FIELD /PLE <<<
     >>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<
      >>> TIMELINESS OF UPDATING IMPROVED - SEE NEWS <<<
>>>NOW AVAILABLE - NEW USER MANUAL GLOBAL PATENT SOURCES - SEE NEWS<<<


L15           257 SEA FILE=WPIDS INSULIN LIKE GROWTH
L16          4149 SEA FILE=WPIDS ISCHAEMI? OR ISCHEMI?
L21        117081 SEA FILE=WPIDS TUBULAR
L23            10 SEA FILE=WPIDS L15(L)(L21 OR L16)


FILE 'BIOSIS' ENTERED AT 09:58:12 ON 04 JAN 96
COPYRIGHT (C) 1996 BIOSIS(R)

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 31 December 1995 (951231/ED)
CAS REGISTRY NUMBERS (R) LAST ADDED: 31 December 1995 (951231/UP)


L24         98468 SEA FILE=BIOSIS ISCHAEMI? OR ISCHEMI?
L25         13546 SEA FILE=BIOSIS INSULIN LIKE GROWTH
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Subheadings - Therapeutic Use - TU
Pharmacology - PD

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L26        29940 SEA FILE=BIOSIS TUBULAR
L27          116 SEA FILE=BIOSIS L25(L)(L24 OR L26)
L28           17 SEA FILE=BIOSIS L27 AND *12512/CC
L31            9 SEA FILE=BIOSIS L28 AND *14508/CC

=> fil capl; d que l49;d que l57; d que l68;s l49 or l57 or l68
FILE 'CAPLUS' ENTERED AT 09:58:17 ON 04 JAN 96
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FILE COVERS 1967 - 4 Jan 1996  VOL 124 ISS 1
FILE LAST UPDATED: 4 Jan 1996  (960104/ED)

  To help control your online searching costs, consider using the
  HCAplus file when using the FSEARCH command or when conducting
  SmartSELECT searches with large numbers of terms.


L44 (      7500) SEA FILE=CAPLUS IGF
L45 (      9740) SEA FILE=CAPLUS INSULIN LIKE
L46 (         5) SEA FILE=REGISTRY ("INSULIN-LIKE GROWTH FACTOR"/CN OR "IN
                   SULIN-LIKE GROWTH FACTOR (HUMAN CLONE PLS32TSC PRECURSOR)
                   "/CN OR "INSULIN-LIKE GROWTH FACTOR 1"/CN OR "INSULIN-LIK
                   E GROWTH FACTOR 1 (PIG)"/CN OR "INSULIN-LIKE GROWTH FACTO
                   R 2"/CN)
L47 (      7983) SEA FILE=CAPLUS L46
L48 (       852) SEA FILE=CAPLUS NECROSIS(5A)TUBULAR
L49            3 SEA FILE=CAPLUS (L44 OR L45 OR L47) AND L48


L50 (      7500) SEA FILE=CAPLUS IGF
L51 (      9740) SEA FILE=CAPLUS INSULIN LIKE
L52 (         5) SEA FILE=REGISTRY ("INSULIN-LIKE GROWTH FACTOR"/CN OR "IN
                   SULIN-LIKE GROWTH FACTOR (HUMAN CLONE PLS32TSC PRECURSOR)
                   "/CN OR "INSULIN-LIKE GROWTH FACTOR 1"/CN OR "INSULIN-LIK
                   E GROWTH FACTOR 1 (PIG)"/CN OR "INSULIN-LIKE GROWTH FACTO
                   R 2"/CN)
L53 (      7983) SEA FILE=CAPLUS L52
L54 (     26754) SEA FILE=CAPLUS ISCHEMI?
L55 (    299066) SEA FILE=CAPLUS RECOVER?
L56 (      1710) SEA FILE=CAPLUS L54(S)L55
L57            6 SEA FILE=CAPLUS L56 AND (L50 OR L51 OR L53)


L58 (      7500) SEA FILE=CAPLUS IGF
L59 (      9740) SEA FILE=CAPLUS INSULIN LIKE
L60 (         5) SEA FILE=REGISTRY ("INSULIN-LIKE GROWTH FACTOR"/CN OR "IN
                   SULIN-LIKE GROWTH FACTOR (HUMAN CLONE PLS32TSC PRECURSOR)
                   "/CN OR "INSULIN-LIKE GROWTH FACTOR 1"/CN OR "INSULIN-LIK
                   E GROWTH FACTOR 1 (PIG)"/CN OR "INSULIN-LIKE GROWTH FACTO
                   R 2"/CN)
L61 (      7983) SEA FILE=CAPLUS L60
L62 (     26754) SEA FILE=CAPLUS ISCHEMI?
L63 (      9672) SEA FILE=CAPLUS L62(S)(INHIBIT? OR PREVENT? OR REDUC? OR
                   DECREAS?)
L68           14 SEA FILE=CAPLUS L63 (L) (L58 OR L59 OR L61)
```

protein or peptide, which comprises exposing a recombinant cons comprising (a) the NGF promotor and (b) a nucleotide encoding th protein or peptide, to a substance which regulates the expressio NGF. The protein or peptide is e.g. NGF, BDNF, CNTF, neurotrophin choline acetyltransferase or transforming growth factor beta 1.

USE/ADVANTAGE - In the treatment of dementia, Alzheimer's disease, damage to the nervous system from trauma, **ischaemia**, toxic agents or infection, or learning disorders. The pref. metho of amin. is by intracerebroventricular injection. @(63pp Dwg.No.0/21)

L75 ANSWER 2 OF 41 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 92-268388 [32] WPIDS
DNC C92-119696
TI Use of **insulin like growth** factor I (IGF-I) to treat cardiac disorders - e.g. cardio-myopathy following drug admin., inflammation, infection, sepsis or **ischaemia**, also to improve reduced cardiac output.
DC B04
IN GLUCKMAN, P; SKOTTNER, A
PA (KABI) KABI PHARMACIA AB; (PHAA) PHARMACIA AB
CYC 26
PI WO 9211865 A1 920723 (9232)* EN 29 pp
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: AU CA FI HU JP KR NO RU US
EP 501937 A1 920902 (9236) EN 16 pp
R: PT
AU 9211669 A 920817 (9245)
ZA 9109977 A 920930 (9245) 26 pp
EP 566641 A1 931027 (9343) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
JP 06504286 W 940519 (9424) 9 pp
AU 657729 B 950323 (9519)
US 5434134 A 950718 (9534) 9 pp
ADT WO 9211865 A1 WO 92-SE9 920110; EP 501937 A1 EP 92-850004 920110; AU 9211669 A AU 92-11669 920110, WO 92-SE9 920110; ZA 9109977 A ZA 91-9977 911219; EP 566641 A1 EP 92-903240 920110, WO 92-SE9 920110; JP 06504286 W JP 92-503611 920110, WO 92-SE9 920110; AU 657729 B AU 92-11669 920110; US 5434134 A WO 92-SE9 920110, US 93-84232 931007
FDT AU 9211669 A Based on WO 9211865; EP 566641 A1 Based on WO 9211865; JP 06504286 W Based on WO 9211865; AU 657729 B Previous Publ. AU 9211669, Based on WO 9211865; US 5434134 A Based on WO 9211865
PRAI SE 91-99 910111
AB WO 9211865 A UPAB: 951004
Use of human **insulin-like growth** factor-I (IGF-I) or analogues for mfg. a medicament for promoting synthesis of cardiac muscle, or treating cardiomyopathies, acute heart failue, myocarditis or myocardial infarction, is new. Also claimed are: (1) a compsn. comprising IGF-I or analogues with additional protein or peptides for enhancing the desired effect(s) of IGF-I, for treating cardiac disorders or promoting cardiac muscle synthesis; (2) a method for promoting cardiac muscle synthesis or treating cardiac disorders by administering IGF-I or analogues; (3) a method for preparing a medicament by combining an effective amt. of IGF-I or analogue and a carrier or diluent.

USE - The IGF-I, or analogues, is useful for treating cardiac disorders such as cardiomyopathies, following drug admin.,

L73 19 L49 OR L57 OR L68

=> dup rem l14,l73,l23,l31
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PROCESSING COMPLETED FOR L73
PROCESSING COMPLETED FOR L23
PROCESSING COMPLETED FOR L31
L74 41 DUP REM L14 L73 L23 L31 (14 DUPLICATES REMOVED)

=> sort py a l74 1-41
PROCESSING COMPLETED FOR L74
L75 41 SORT L74 1-41 PY A — sort by publication year, ascending order

=> d bib ab l75 1-30; d bib l75 31-41 — abstracts can be printed for any of these that are of particular interest

L75 ANSWER 1 OF 41 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 91-073542 [10] WPIDS
DNC C91-031179
TI Regulating levels of MGF in CNS by admin. various cytokines - useful e.g. for treating dementia, alzheimer's disease or nerve damage.
DC B04 D16
IN HENGERER, B; LINDHOLM, D B; THOENEN, H
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN; (PLAN-N) PLANCK INST PSYCHIATRY INST MAX
CYC 14
PI WO 9102067 A 910221 (9110)*
RW: AT BE CH DE DK ES FR GB IT LU NL SE
EP 484416 A 920513 (9220) EN 63 pp
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
JP 05025056 A 930202 (9310)
ADT EP 484416 A EP 90-911746 900727; JP 05025056 A JP 90-198053 900727
FDT EP 484416 A Based on WO 9102067
PRAI US 89-386546 890727; US 90-555006 900720
AB WO 9102067 A UPAB: 930928
A new method for regulating the levels of nerve growth factor (NGF) in the central nervous system is claimed, which comprises administering a cytokine. the cytokine is selected from interleukin 1, fibroblast growth factor, tumour growth factor alpha or beta, platelet derived growth factor or **insulin-like growth** factor I or II. The levels of NGF can also be regulated by administering interleukin-1 inhibitor, glucocorticoid or dexamethasone, which act by altering levels of cytokine in the body.

Also claimed is a method for controlling the expression of a

Journal code: 3U8. ISSN: 0002-9513.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9410

AB Insulin-like growth factor I (IGF-I) improves kidney function and histopathology, when given within a short time (0.5 or 5 h) after an ischemic renal insult in rats. To examine the effects of IGF-I at times that would be more applicable if it were to be used as a therapeutic agent for acute renal failure in humans, we administered IGF-I to rats 24 h after ischemic injury or prior to the induction of injury (pretreatment). In rats that received IGF-I 24 h postischemia, serum creatinine and blood urea nitrogen (BUN) values were significantly lower during the subsequent 6 days than in vehicle-treated rats, and incorporation of 5-bromo-2'-deoxyuridine into tubular cells of the regenerating cortex, measured 48 h postischemia, was enhanced. When examined 7 days postinjury, kidneys from rats that received IGF-I 24 h postischemia were improved in histopathological appearance compared with kidneys from vehicle-treated animals. Whereas creatinine and BUN values were elevated above baseline in both vehicle and IGF-I-pretreated groups, recovery of normal renal function was accelerated by pretreatment with IGF-I. In addition, although we could detect no differences in histopathology at 24 h postinjury, IGF-I pretreatment resulted in more normal renal histology at 7 days postischemic injury and reduced weight loss after injury. Our data show that IGF-I hastens recovery and accelerates regeneration or repair of damaged epithelia following acute renal failure in rats when administered either 24 h postinjury or prior to induction of acute renal failure.(ABSTRACT TRUNCATED AT 250 WORDS)

L75 ANSWER 30 OF 41 MEDLINE
AN 94186754 MEDLINE
TI Effects of insulin-like growth factor-I peptides in rats with acute renal failure.
AU Martin A A; Gillespie C M; Moore L; Ballard F J; Read L C
CS Cooperative Research Centre for Tissue Growth and Repair, Child Health Research Institute, North Adelaide, Australia.
SO J Endocrinol, (1994 Jan) 140 (1) 23-32.
Journal code: I1J. ISSN: 0022-0795.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9406
AB The effect of insulin-like growth factor-I (IGF-I) administration on body weight gain and the rate of recovery of renal function was investigated in rats following an acute episode of renal ischaemia. Since the des(1-3)IGF-I and LR3IGF-I variant forms of IGF-I have been shown to be more potent than IGF-I, their effects were also examined. Acute renal failure was produced in male Sprague-Dawley rats by clamping both renal arteries for 45 min. Treatment was commenced at the time of renal artery occlusion with vehicle (0.1 mol acetic acid/l; control group), IGF-I (2.0 mg/kg per day), des(1-3)IGF-I (2.0 mg/kg per day) or LR3IGF-I (1.5 mg/kg per day) by s.c. osmotic pump, and continued for 7 days, with rats being held in

metabolism cages. Glomerular filtration rate (GFR) was estimated by the use of 51Cr-EDTA continuously infused i.p. via osmotic pump. Following the episode of renal ischaemia, body weight gain and nitrogen retention were significantly improved in all three peptide-treated groups, and serum urea concentrations were reduced in the groups treated with IGF-I and des(1-3)IGF-I. However, there was no evidence of the variants having any increased potency over the growth effects of IGF-I itself. GFR was significantly reduced, urine output was increased and urinary concentrating ability was reduced in all groups compared with normal rats, with no significant effect of the IGF peptides being apparent. A closer examination of the acute effects of LR3IGF-I on renal function was undertaken by measuring GFR for 3 days before and 3 days after renal ischaemia in two groups of rats, treated for the latter 3 days with either vehicle (controls) or LR3IGF-I (1.5 mg/kg per day). LR3IGF-I treatment following renal ischaemia resulted in a significantly greater fall in GFR than in controls, urinary osmolality was also significantly reduced, and fractional excretion of sodium was increased. In addition, there was histological evidence of a greater degree of tubular epithelial calcification in the kidneys of the rats treated with LR3IGF-I. This study showed that administration of IGF peptides at doses sufficient to cause significant improvement in anabolic status did not improve renal function in rats following an acute episode of renal ischaemia. Indeed the LR3IGF-I variant of IGF-I had a deleterious effect on renal function in the early stage of the recovery period.

L75 ANSWER 31 OF 41 MEDLINE
AN 94156991 MEDLINE
TI Intraventricular administration of insulin and IGF-1 in transient forebrain ischemia.
AU Zhu C Z; Auer R N
CS Neuroscience Research Group, University of Calgary, Alberta, Canada.
SO J Cereb Blood Flow Metab, (1994 Mar) 14 (2) 237-42.
Journal code: HNL. ISSN: 0271-678X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9406

L75 ANSWER 32 OF 41 BIOSIS COPYRIGHT 1996 BIOSIS
AN 94:465127 BIOSIS
DN 97478127
TI The role of IGF-I in the response to organ injury-studies in the central nervous system.
AU Gluckman P D; Williams C E; Guan J; Beilharz E; Johnston B M
CS Research Centre Developmental Med. Biol., Univ. Auckland, Private Bag 92019, Auckland, NEZ
SO Baxter, R. C., P. D. Gluckman and R. G. Rosenfeld (Ed.). International Congress Series, No. 1056. The insulin-like growth factors and their regulatory proteins; Third International Symposium, Sydney, New South Wales, Australia, February 6-10, 1994. x+474p. Elsevier Science Publishers B.V.: Amsterdam, Netherlands; New York, New York, USA. 0 (0). 1994. 427-434. ISBN: 0-444-81756-5

DT Book; Conference
LA English

L75 ANSWER 33 OF 41 BIOSIS COPYRIGHT 1996 BIOSIS
AN 94:242013 BIOSIS
DN 97255013
TI In vivo neurotrophic activity of rhIGF-I on motor neurons and nerves: A potential treatment for ALS.
AU Vaught J L; Hantai D; Blonde B; Rieger F; Contreras P C
CS Cephalon, Inc., West Chester, PA, USA
SO Experimental Biology 94, Parts I and II, Anaheim, California, USA, April 24-28, 1994. FASEB Journal 8 (4-5). 1994. A657. ISSN: 0892-6638
DT Conference
LA English

L75 ANSWER 34 OF 41 BIOSIS COPYRIGHT 1996 BIOSIS
AN 94:196766 BIOSIS
DN 97209766
TI Neuronal rescue after hypoxic **ischemic** injury (HI) using **insulin-like growth** factor-1.
AU Gluckman P D; Williams C E; Bielharz E; Guan J
CS Research Center Developmental Med. Biol., Sch. Med., Auckland, NEZ
SO Annual Meeting of the European Society for Paediatric Research, Edinburgh, Scotland, UK, September 12-16, 1993. Pediatric Research 35 (2). 1994. 263. ISSN: 0031-3998
DT Conference
LA English

L75 ANSWER 35 OF 41 CAPLUS COPYRIGHT 1996 ACS
AN 1995:816175 CAPLUS
DN 123:218502
TI Role of neurotrophic factors in ischemic brain damage
AU Lindholm, D.; Beck, T.
CS Dept Neurochemistry, Max Planck Institute Psychiatry, Munich, D-82152, Germany
SO Pharmacol. Cereb. Ischemia 1994, [Int. Symp.], 5th (1994), 385-8. Editor(s): Krieglstein, Josef; Oberpichler-Schwenk, Heike. Publisher: Medpharm Scientific Publishers, Stuttgart, Germany. CODEN: 61RMAY
DT Conference; General Review
LA English

L75 ANSWER 36 OF 41 CAPLUS COPYRIGHT 1996 ACS
AN 1994:401498 CAPLUS
DN 121:1498
TI Centrally administered insulin and IGF-1 in transient forebrain ischemia in fasted rats
AU Zhu, C. Z.; Auer, R. N.
CS Dep. Pathol. and Clin. Neurosci., Univ. Calgary, Calgary, AB, T2N 4N1, Can.
SO Neurol. Res. (1994), 16(2), 116-20 CODEN: NRESDZ; ISSN: 0161-6412
DT Journal
LA English

L75 ANSWER 37 OF 41 MEDLINE

95372413 MEDLINE
Cardioprotective effect of insulin-like growth factor I in myocardial ischemia followed by reperfusion.
Buerke M; Murohara T; Skurk C; Nuss C; Tomaselli K; Lefer A M
Department of Physiology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA 19107, USA.
GM-45434 (NIGMS)
Proc Natl Acad Sci U S A, (1995 Aug 15) 92 (17) 8031-5.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9511

L75 ANSWER 38 OF 41 MEDLINE
AN 95306748 MEDLINE
TI Insulin-like growth factor-1 (IGF-1) enhances recovery from HgCl2-induced acute renal failure: the effects on renal IGF-1, IGF-1 receptor, and IGF-binding protein-1 mRNA.
AU Friedlaender M; Popovtzer M M; Weiss O; Nefesh I; Kopolovic J; Raz I
CS Nephrology Service, Hadassah University Hospital, Jerusalem, Israel.
SO J Am Soc Nephrol, (1995 Apr) 5 (10) 1782-91.
Journal code: A6H. ISSN: 1046-6673.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9509

L75 ANSWER 39 OF 41 MEDLINE
AN 95287126 MEDLINE
TI Insulin-like growth factor-1 enhances epidermal growth factor receptor activation and renal tubular cell regeneration in postischemic acute renal failure [see comments].
CM Comment in: J Lab Clin Med 1995 Jun;125(6):684-5
AU Lin J J; Cybulsky A V; Goodyer P R; Fine R N; Kaskel F J
CS Department of Pediatrics, State University of New York at Stony Brook 11794, USA.
SO J Lab Clin Med, (1995 Jun) 125 (6) 724-33.
Journal code: IVR. ISSN: 0022-2143.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 9509

L75 ANSWER 40 OF 41 CAPLUS COPYRIGHT 1996 ACS
AN 1995:734270 CAPLUS
DN 123:195178
TI Renal tubule cell repair following acute renal injury
AU Humes, H. David; Lake, Edward W.; Liu, Shigang
CS VA Medical Center, Univ. Michigan, Ann Arbor, MI, USA
SO Miner. Electrolyte Metab. (1995), 21(4-5), 353-65
CODEN: MELMDI; ISSN: 0378-0392
DT Journal; General Review
LA English

L75 ANSWER 41 OF 41 CAPLUS COPYRIGHT 1996 ACS
AN 1995:675613 CAPLUS
DN 123:166627
TI Renal growth hormone-**insulin-like** growth factor-I system in acute renal failure
AU Tsao, Tanny; Wang, Jin; Fervenza, Fernando C.; Vu, Thanh H.; Jin, Isabella H.; Hoffman, Andrew R.; Rabkin, Ralph
CS Department Veterans Affairs Medical Center, Stanford University, Palo Alto, CA, USA
SO Kidney Int. (1995), 47(6), 1658-68
CODEN: KDYIA5; ISSN: 0085-2538
DT Journal
LA English

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il wpids; d que l37; fil biosis; d que l34
 'WPIDS' ENTERED AT 10:00:15 ON 04 JAN 96
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LE LAST UPDATED: 21 DEC 95                    <951221/UP>
>UPDATE WEEKS:
OST RECENT DERWENT WEEK                 9551   <199551/DW>
ERWENT WEEK FOR CHEMICAL CODING:        9539
DERWENT WEEK FOR POLYMER INDEXING:      9546
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
>>> DERWENT POLYMER INDEXING THESAURUS AVAILABLE IN FIELD /PLE <<<
     >>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<
      >>> TIMELINESS OF UPDATING IMPROVED - SEE NEWS <<<
>>>NOW AVAILABLE - NEW USER MANUAL GLOBAL PATENT SOURCES - SEE NEWS<<<


L15          257 SEA FILE=WPIDS INSULIN LIKE GROWTH
L16         4149 SEA FILE=WPIDS ISCHAEMI? OR ISCHEMI?
L18         8000 SEA FILE=WPIDS RENAL OR KIDNEY#
L36          694 SEA FILE=WPIDS CYTOKINE#
L37            1 SEA FILE=WPIDS L15 AND (L16 OR L18) AND L36


FILE 'BIOSIS' ENTERED AT 10:00:19 ON 04 JAN 96
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 31 December 1995 (951231/ED)
CAS REGISTRY NUMBERS (R) LAST ADDED: 31 December 1995 (951231/UP)


L24         98468 SEA FILE=BIOSIS ISCHAEMI? OR ISCHEMI?
L25         13546 SEA FILE=BIOSIS INSULIN LIKE GROWTH
L26         29940 SEA FILE=BIOSIS TUBULAR
L27           116 SEA FILE=BIOSIS L25(L)(L24 OR L26)
L32         31541 SEA FILE=BIOSIS CYTOKINE#
L34             1 SEA FILE=BIOSIS L27 AND L32

=> dup rem l34,l37
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PROCESSING COMPLETED FOR L34
PROCESSING COMPLETED FOR L37
L76             2 DUP REM L34 L37 (0 DUPLICATES REMOVED)

=> d bib ab l76 1-2;fil hom

L76  ANSWER 1 OF 2  BIOSIS  COPYRIGHT 1996 BIOSIS
AN  94:519391  BIOSIS
DN  97532391
```

TI **Insulin-like growth** factor-1 (IgF-1) reduces **cytokine** and MHC induction after acute **tubular** necrosis (ATN).
AU Goes N; Urmson J; Ramassar V; Halloran P F
CS Univ. Alberta, Edmonton, AB T6G 2R8, CAN
SO Abstracts Submitted for the 27th Annual Meeting of the American Society of Nephrology, Orlando, Florida, USA, October 26-29, 1994. Journal of the American Society of Nephrology 5 (3). 1994. 897. ISSN: 1046-6673
DT Conference
LA English

L76 ANSWER 2 OF 2 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 91-073542 [10] WPIDS
DNC C91-031179
TI Regulating levels of MGF in CNS by admin. various **cytokines** - useful e.g. for treating dementia, alzheimer's disease or nerve damage.
DC B04 D16
IN HENGERER, B; LINDHOLM, D B; THOENEN, H
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN; (PLAN-N) PLANCK INST PSYCHIATRY INST MAX
CYC 14
PI WO 9102067 A 910221 (9110)*
RW: AT BE CH DE DK ES FR GB IT LU NL SE
EP 484416 A 920513 (9220) EN 63 pp
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
JP 05025056 A 930202 (9310)
ADT EP 484416 A EP 90-911746 900727; JP 05025056 A JP 90-198053 900727
FDT EP 484416 A Based on WO 9102067
PRAI US 89-386546 890727; US 90-555006 900720
AB WO 9102067 A UPAB: 930928
A new method for regulating the levels of nerve growth factor (NGF) in the central nervous system is claimed, which comprises administering a **cytokine**. the **cytokine** is selected from interleukin 1, fibroblast growth factor, tumour growth factor alpha or beta, platelet derived growth factor or **insulin-like growth** factor I or II. The levels of NGF can also be regulated by administering interleukin-1 inhibitor, glucocorticoid or dexamethasone, which act by altering levels of **cytokine** in the body.

Also claimed is a method for controlling the expression of a protein or peptide, which comprises exposing a recombinant construct comprising (a) the NGF promotor and (b) a nucleotide encoding the protein or peptide, to a substance which regulates the expression of NGF. The protein or peptide is e.g. NGF, BDNF, CNTF, neurotrophin-3, choline acetyltransferase or transforming growth factor beta 1.

USE/ADVANTAGE - In the treatment of dementia, Alzheimer's disease, damage to the nervous system from trauma, **ischaemia**, toxic agents or infection, or learning disorders. The pref. method of amin. is by intracerebroventricular injection. @(63pp Dwg.No.0/21)

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determine whether IGF-I affects glomerular filtration rate and renal plasma flow in humans with reduced renal function, we administered recombinant human IGF-I (rhIGF-1) to patients with moderate chronic renal failure. Four patients whose baseline inulin clearances were 21.9, 23.2, 34.9, and 55.1 ml.cntdot.min-1.cntdot.1.73 M-2 were placed on a 1 g.cntdot. kg-1.cntdot.day-1 protein diet and studied over a 10-day period (0-10). On days 4-7, 100 .mu.g/kg of rhIGF-I was subcutaneously administered twice daily to the patients. The effects of rhIGF-I on levels of circulating IGF-I, inulin clearance, p-aminohippurate (PAH) clearance, kidney volume, plasma glucose, plasma and urine calcium and phosphate, and urine sodium and protein were determined. Administration of rhIGF-I increased levels of circulating IGF-I, inulin clearances, PAH clearances, and kidney size in each of the four patients receiving the growth factor. IGF-I did not cause weight gain, natriuresis, proteinuria, or hypoglycemia. Plasma calcium and phosphate were not affected by rhIGF-I. However, the percent **tubular** reabsorption of filtered phosphate was increased. We conclude that administration of rhIGF-I can enhance glomerular filtration rate and renal plasma flow at least in some humans with moderately reduced renal function. The enhancement is associated with an increase in kidney volume.

L75 ANSWER 21 OF 41 BIOSIS COPYRIGHT 1996 BIOSIS
AN 93:235404 BIOSIS
DN BA95:126579
TI BLOOD PRESSURE AND THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM IN CHILDREN RECEIVING RECOMBINANT HUMAN GROWTH HORMONE.
AU BARTON J S; HINDMARSH P C; PREECE M A; BROOK C G D
CS INST. CHILD HEALTH, 30 GUILFORD ST., LONDON WC1N 1EH, UK.
SO CLIN ENDOCRINOL 38 (3). 1993. 245-251. CODEN: CLECAP ISSN: 0300-0664
LA English
AB Objective: We investigated the effect of growth hormone (GH) treatment on salt and water metabolism and the renin-angiotensin-aldosterone system in children with short stature. Design: Randomized, controlled study. Patients: Twenty-nine short, pre-pubertal children referred to two specialist growth clinics for further assessment. Measurements: Serial measurements of blood pressure, body weight, plasma renin activity (PRA), aldosterone, electrolytes, insulin and **insulin-like growth** factor I (IGF-I) have been made following the initiation of GH treatment. Results: A small and transient increase in systolic blood pressure was observed during the first week of GH treatment. The increase in blood pressure over baseline was -1.1 mmHg in controls compared to + 11.5 and +3.0 mmHg in children receiving standard (20 units/m2/week) and high dose (40 units/m2/week) GH respectively (P=0.004). Over the same time interval body weight also tended to increase with GH compared with controls. These changes were greater in those children receiving the lower dose of GH and were not significantly related to age or prior GH status. PRA did not change with GH treatment. Although plasma aldosterone concentration tended to increase with GH, maximal values did not differ from controls and all remained within our normal range. Plasma IgF-1 levels were increased by a similar amount in both treatment groups (1.5 and 1.12 U/ml compared to 0.44 U/ml in controls at 4 months). No difference in plasma insulin concentration was noted after 7 days of GH. Conclusions: In contrast to adult subjects, treatment with high dose GH in childhood is not associated with activation of the

nin-angiotensin-aldosterone system. Clinical signs consistent with ansient salt and water retention are observed with GH therapy, owever, suggesting either a direct effect of GH or of IGF-I on renal **tubular** function. Blood pressure, plasma renin activity and plasma aldosterone levels were not increased after more prolonged GH therapy. These data suggest that high dose GH therapy in childhood is unlikely to be associated with the increased risk of hypertension seen in adults with GH hypersecretion.

,75 ANSWER 22 OF 41 CAPLUS COPYRIGHT 1996 ACS
AN 1994:290145 CAPLUS
DN 120:290145
TI Growth factors protect neurons against excitotoxic/ischemic damage by stabilizing calcium homeostasis
AU Mattson, Mark P; Cheng, Bin
CS Sanders-Brown Res. Cent. Aging, Univ. Kentucky, Lexington, KY, 40536-0230, USA
SO Stroke (Dallas) (1993), 24(12, Suppl., Cerebrovascular Diseases), I136-I140
CODEN: SJCCA7; ISSN: 0039-2499
DT Journal; General Review
LA English
AB A review, with 30 refs., describing recent work on the mechanisms of action of growth factors in protecting neurons against ischemia. An aberrant elevation in intraneuronal calcium levels resulting from energy failure and excitatory amino acid receptor activation is believed to play a major role in the neuronal damage and death that occur in stroke. The authors have found that several growth factors can protect cultured rat hippocampal and septal neurons and human cortical neurons from excitotoxic damage caused by glucose deprivation or hypoxia. Using the calcium indicator dye fura 2 and whole-cell patch-clamp recording, the authors found that glucose deprivation initially results in calcium current inhibition and a redn. in intraneuronal free calcium levels without morphol. signs of cell damage. After 12 to 16 h of glucose deprivation, a large elevation in intraneuronal calcium levels occurred that involved N-methyl-D-aspartate receptor activation and mediated the cell damage and death. Basic fibroblast growth factor (bFGF), nerve growth factor (NGF), and **insulin-like** growth factors (**IGF**-I and **IGF**-II) each prevented, in a dose-dependent manner, glucose deprivation-induced loss of calcium homeostasis and neuronal damage. The growth factors were effective to varying degrees when added up to 12 h after the onset of glucose deprivation. NGF, bFGF, and IGFs also protected neurons against damage caused by exposure to a hypoxic environment. By stabilizing intraneuronal calcium levels within a window of concns. conducive to neuronal survival, growth factors can protect neurons against the damaging effects of ischemia-like insults. Because ATP levels are expected to be **reduced** under **ischemia**-like conditions, the authors detd. whether the growth factors would protect neurons against a more selective redn. in ATP levels. Basic FGF, IGFs, and NGF all significantly reduced neuronal damage caused by cyanide or 2,4-dinitrophenol. The authors' data demonstrate that bFGF, NGF, and IGFs can protect central nervous system neurons against **ischemia**-like insults and suggest that these growth factors could **reduce** brain damage in stroke. Understanding the mechanism or mechanisms of action of these growth

factors may reveal mol. targets for the development of drugs use in stroke.

L75 ANSWER 23 OF 41 CAPLUS COPYRIGHT 1996 ACS
AN 1993:557579 CAPLUS
DN 119:157579
TI Altered growth factor expression during toxic proximal **tubular necrosis** and regeneration
AU Verstrepen, Walter A.; Nouwen, Etienne J.; Yue, Xiao S.; De Broe, Marc E.
CS Dep. Nephrol. Hypertens., Univ. Antwerp, Antwerp, Belg.
SO Kidney Int. (1993), 43(6), 1267-79
CODEN: KDYIA5; ISSN: 0085-2538
DT Journal
LA English
AB Growth factor expression was investigated during the regenerative response after toxic proximal **tubular necrosis**. Therefore, gentamicin was administered to rats to achieve an exptl. model. characterized by the appearance of segment-specific proximal **tubular necrosis**, that is followed by a regenerative response leading to functional and morphol. recovery in a limited time. Four days after the administration of the highest dose, serum creatinine rose to a mean value of 5.8 mg/dL and returned to normal values 10 days after the treatment. The S1-S2 segment of the proximal tubules in the cortex became clearly affected by severe toxic necrosis on day after the treatment, while maximal necrosis was obsd. at days 2 to 4. Only minor injuries were noticed in the other renal compartments. The proliferative response stated in the interstitial cells first. The major proliferative wave was localized in the convoluted part of the proximal tubules at days 6 to 8, although proliferation was also prominent among non-proximal tubular cells. A profound interstitial infiltration of leukocytes, including macrophages and T lymphocytes, was obsd. Ten days after the treatment the functional and morphol. recovery were completed. Slot blot hybridization revealed a decreased EGF and **IGF**-I mRNA expression from the start of the observation period. While **IGF**-I mRNA had regained its normal expression at day 10, EGF mRNA was still below control levels. The PDGF-B transcript became more abundant towards the end of the authors' observations. No major change in the expression ot TGF-.alpha., TGF-.beta.1 and c-fos were detected. Renal EGF-immunoreactivity disappeared from the luminal plasma membrane of the distal tubular cells analogous to the results obtained at the messenger level. However, EGF-staining was lost in the cortex first, hence a topog. assocn. between the loss of EGF-immunoreactivity in the distal tubules and the obsd. necrotic lesions in the proximal tubular cells from normal, injured or regenerating rat kidneys. In this exptl. rat model, EGF and **IGF**-I mRNA expression is apparently decreased during the regenerative response upon severe toxic **tubular necrosis**. No evidence for a participation of EGF or **IGF**-I of renal origin in the recovery of the kidney is found.

L75 ANSWER 24 OF 41 CAPLUS COPYRIGHT 1996 ACS
AN 1993:469574 CAPLUS
DN 119:69574

of drugs useful

differential expression of **insulin-like** growth factor binding proteins (IGFBP) 4 and 5 mRNA in the rat brain after transient hypoxic-ischemic injury
Beilharz, Erica J.; Klempt, Nicolin D.; Klempt, Martin; Sirimanne, Ernest; Dragunow, Mike; Gluckman, Peter D.
Res. Cent. Dev. Med. and Biol., and, Auckland, N. Z.
Mol. Brain Res. (1993), 18(3), 209-15
CODEN: MBREE4; ISSN: 0169-328X
DT Journal
LA English
AB **Insulin-like** growth factor (**IGF**) system may have a role in the repair of damaged cerebral tissues following hypoxic-ischemic injury in the infant rat brain. A unilateral model of hypoxic-ischemic injury was used to assess the involvement of two **IGF** binding proteins, IGFBP-4 and IGFBP-5, in the post-asphyxial response. Ligation of the right carotid artery of 21-day-old rats was followed by 15 or 60 min exposure to 8% oxygen to produce moderate or severe damage, resp. Using in situ hybridization, the distribution of IGFBP-4 and IGFBP-5 mRNA was detd. in brains collected over 10 days following the insult. In the control brains (no damage), both IGFBPs were expressed in distinct regions. IGFBP-4 mRNA was detected in limited areas of the hippocampus and in several cortical layers, while IGFBP-5 mRNA was found primarily in the thalamus. In response to hypoxic-**ischemic** injury, IGFBP-4 mRNA expression was **reduced** in regions of neuronal loss, suggesting a neuronal origin for IGFBP-4. The expression of IGFBP-5 mRNA was not altered by the 15-min insult, but was heavily induced from 3 days following the 60-min insult, particularly in the subependymal layer and adjacent white matter on the ligated hemisphere. IGFBP-5 may be involved in the **recovery** from severe hypoxic-**ischemic** injury and may be important in the regeneration of oligodendrocytes.

L75 ANSWER 25 OF 41 CAPLUS COPYRIGHT 1996 ACS
AN 1993:463949 CAPLUS
DN 119:63949
TI Basic FGF, NGF, and IGFs protect hippocampal and cortical neurons against iron-induced degeneration
AU Zhang, Ying; Tatsuno, Tohru; Carney, John M.; Mattson, Mark P.
CS Sanders-Brown Res. Cent. Aging, Univ. Kentucky, Lexington, KY, 40536-0230, USA
SO J. Cereb. Blood Flow Metab. (1993), 13(3), 378-88
CODEN: JCBMDN; ISSN: 0271-678X
DT Journal
LA English
AB Iron is believed to contribute to the process of cell damage and death resulting from ischemic and traumatic insults by catalyzing the oxidn. of protein and lipids. Exposure of cultured rat hippocampal neurons to iron (FeSO4) caused a dose-dependent redn. in neuronal survival, which was potentiated by ascorbate. Damage to neurons was assocd. with a significant level of oxygen radical in the culture medium. The iron chelator desferal prevented both the neuronal degeneration caused by FeSO4 and the prodn. of oxygen radical, demonstrating that ionic iron was responsible for the cell damage. Iron neurotoxicity was assocd. with an elevation of [Ca2+]i and was attenuated by NMDA receptor antagonists. Since recent

findings demonstrated neuroprotective effects of growth factors in cell culture and in vivo models of ischemia, the effects of growth factors on iron-induced damage were studied. Basic fibroblast growth factor (bFGF), nerve growth factor (NGF), and **insulin -like** growth factors (**IGF**-I and **IGF** -II) each protected neurons against iron-induced damage. Both rat hippocampal and human cortical neurons were protected by these growth factors. Taken together, the data suggest that the neuroprotective effects of growth factors against excitotoxic/ **ischemic** insults may result, in part, from a **prevention** or attenuation of oxidative damage.

L75 ANSWER 26 OF 41 MEDLINE
AN 95118750 MEDLINE
TI What are the clinical uses of insulin-like growth factor-I in acute and chronic renal failure?.
AU Hammerman M R
CS Renal Division Washington University School of Medicine, St. Louis, MO 63110.
SO Pediatr Nephrol, (1994 Oct) 8 (5) 544.
Journal code: AVR. ISSN: 0931-041X.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9504

L75 ANSWER 27 OF 41 MEDLINE
AN 95035890 MEDLINE
TI Therapeutic use of growth factors in renal failure [editorial].
AU Hammerman M R; Miller S B
NC DK-45181 (NIDDK)
DK-27600 (NIDDK)
DK-20579 (NIDDK)
+
SO J Am Soc Nephrol, (1994 Jul) 5 (1) 1-11. Ref: 71
Journal code: A6H. ISSN: 1046-6673.
CY United States
DT Editorial
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 9502
AB Polypeptide growth factors regulate kidney development, growth, and function and participate in processes of repair after renal injury. The use of one or more growth factors as therapeutic agents has been proposed in the settings of acute and chronic renal failure. In animal models of acute renal injury, the administration of epidermal growth factor, insulin-like growth factor I (IGF-I), or hepatocyte growth factor accelerates the restoration of kidney function and the normalization of histology post-acute renal injury and reduces mortality. The mechanisms by which the growth factors act in acute renal failure include the stimulation of anabolism, the maintenance of glomerular filtration, and the enhancement of tubular regeneration. IGF-I has been safely administered to humans with chronic renal failure. The growth factor enhances GFR and RPF in

these individuals. Further studies will be required to establish a role for IGF-I or other growth factors as therapeutic agents for acute renal failure in humans and to define the utility of IGF-I as a medical therapy for chronic renal insufficiency.

ANSWER 28 OF 41 MEDLINE
94340877 MEDLINE
Recovery from acute ischaemic renal failure is accelerated by des-(1-3)-insulin-like growth factor-1.
AU Clark R; Mortensen D; Rabkin R
CS Department of Endocrine Research, Genentech, Inc., San Francisco, California.
NC RO1-DK 32342 (NIDDK)
SO Clin Sci (Colch), (1994 Jun) 86 (6) 709-14.
Journal code: DIZ. ISSN: 0143-5221.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9411
AB 1. Acute renal failure carries a high risk of morbidity and mortality, so there is a need for agents that minimize renal injury after an insult and that hasten repair. Insulin-like growth factor-1 is mitogenic for renal tubular cells; in normal kidneys it has haemodynamic effects and it is potently anabolic. We tested the theory that insulin-like growth factor-1 may be of use in the treatment of acute renal failure by administering recombinant des-(1-3)-insulin-like growth factor-1, a truncated form of insulin-like growth factor-1, which occurs naturally. Ischaemic renal failure was induced in normal rats by occluding both renal pedicles for 60 min. Then des-(1-3)-insulin-like growth factor-1 (0.8 mg day-1 kg-1) or vehicle was given by subcutaneous minipump for 7 days. The rats were weighed and bled daily and in one experiment were housed in metabolic cages and urine was collected. 2. Des-(1-3)-insulin-like growth factor-1 caused a lower and earlier peak in both serum creatinine and blood urea-nitrogen levels, and a more rapid and complete return toward basal values than in untreated animals. Also des-(1-3)-insulin-like growth factor-1 significantly increased creatinine clearance and reduced fractional excretion of filtered sodium. Besides these beneficial effects on kidney function, des-(1-3)-insulin-like growth factor-1 was anabolic as treated rats gained weight while control rats lost weight. The mortality in control rats was 28% compared with 6% in treated rats.(ABSTRACT TRUNCATED AT 250 WORDS)

L75 ANSWER 29 OF 41 MEDLINE
AN 94295744 MEDLINE
TI Rat models for clinical use of insulin-like growth factor I in acute renal failure.
AU Miller S B; Martin D R; Kissane J; Hammerman M R
CS Department of Internal Medicine, Washington University School of Medicine, St. Louis, Missouri 63110.
NC DK-45181 (NIDDK)
DK-07126 (NIDDK)
DK-27600 (NIDDK)
+
SO Am J Physiol, (1994 Jun) 266 (6 Pt 2) F949-56.

inflammation, infection, sepsis or **ischaemia**. It is also useful for improving cardiac output, e.g. by improving shoke vol.
The dosage of IGF-I given is 0.01-10 (pref. 0.1-2) mg/kg body wt./day, administered s.c. (pref.), intramuscularly, i.v., intranasally, orally or dermally or by a combination of rout
Dwg. 0/3
Dwg. 0/3

L75 ANSWER 3 OF 41 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 93-076174 [09] WPIDS
DNC C93-033553
TI Treatment and prevention of central nervous system damage using IGF-1 - for hypoxic, ischaemic and traumatic injury to glia and other non-cholinergic cells.
DC B04
IN GLUCKMAN, P; NIKOLICS, K
PA (AUCK-N) AUCKLAND UNISERVICES LTD; (GETH) GENENTECH INC
CYC 19
PI WO 9302695 A1 930218 (9309)* EN 28 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE
W: CA JP US
EP 597033 A1 940518 (9420) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE
ADT WO 9302695 A1 WO 92-US6389 920803; EP 597033 A1 EP 92-917908 920803, WO 92-US6389 920803
FDT EP 597033 A1 Based on WO 9302695
PRAI NZ 91-239211 910801
AB WO 9302695 A UPAB: 931119
Method for treating CNS injury affecting glia or other non-cholinergic cells in a mammal, comprises administering to the CNS of the mammal **insulin-like growth** factor (IGF)-1 and/or a biologically active analogue of IGF-1.
The IGF-1 analogue may be e.g. IGF-2 or truncated IGF-1 (des 1-3 IGF-1).
USE - To reduce the severity of CNS damage by reducing infarction and loss of glial cells and non-cholinergic neuronal cells after a CNS insult. The method can be used to prevent or treat CNS damage associated with asphyxia, hypoxia, toxins, infarction, **ischaemia** or trauma or as a consequence of Parkinson's disease, multiple sclerosis or a demyelinating disorder.
Dwg.0/8

L75 ANSWER 4 OF 41 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 93-167391 [20] WPIDS
DNC C93-074608
TI Neurotrophic factors e.g. BFGF, AFGF and CNTF - used to induce trophic effects on brain cells, brain glial cells and blood vessels, for treating and preventing neuronal damage.
DC B04
IN ALPS, B J; BROWN, C M; COLLINS, F D; EMMETT, C J; FINKLESTEIN, S P; MOSKOWITZ, M A; RUSSELL, D; SPEDDING, M; WHITING, R L
PA (GEHO) GEN HOSPITAL CORP; (SYNT) SYNTEX-SYNERGEN NEUROSCIENCE JOINT VENTU
CYC 37
PI WO 9308828 A1 930513 (9320)* EN 52 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA SE
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK LU MG

Also claimed are: (B) a soln. of IGF-I or IGF-II or functional deriv. in an excipient for ophthalmic administration, the soln. being contained within a chemically inert vessel which is (i) closed at one end with a device for the transfer of drops of the soln. from the vessel to an eye of a patient or (ii) implanted into a patient for the transfer of the soln. from the vessel to an eye of the patient; (c) an ointment contg. IGF-I, IGF-II or a functional deriv. in an excipient for ophthalmic admin; (D) a pure peptide comprising a sequence selected from sequences (I)-(III) ALLETYSATPAKSE (I), ETQCATPAKSE (II), GAELVDALQFYSGDRGFYFNKPTG (III).

USE/ADVANTAGE - The IGF-I, IGF-II and their derivs. function to promote the survival of retinal neuronal cells. They can be used for the treatment of retinal neuronal tissues which are suffering from the effects of injury, aging and/or disease such as photodegeneration, trauma, axotomy, neurotoxic-excitatory degeneration, **ischaemic** neuronal degeneration etc.
Dwg.0/11

L75 ANSWER 6 OF 41 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 93-182242 [22] WPIDS
DNC C93-080677
TI Treatment of central nervous system injury - by using transforming growth factor beta-1, e.g. for treating hypoxic, traumatic or ischaemic injury.
DC B04
IN GLUCKMAN, P; NIKOLICS, K; WILLIAMS, C
PA (AUCK-N) AUCKLAND UNISERVICES LTD; (GETH) GENENTECH INC
CYC 19
PI WO 9309802 A2 930527 (9322)* EN 14 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE
W: CA JP US
EP 625050 A1 941123 (9445) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE
JP 07501080 W 950202 (9514)
ADT WO 9309802 A2 WO 92-US9974 921120; EP 625050 A1 EP 92-925330 921120, WO 92-US9974 921120; JP 07501080 W WO 92-US9974 921120, JP 93-509515 921120
FDT EP 625050 A1 Based on WO 9309802; JP 07501080 W Based on WO 9309802
PRAI NZ 91-240696 911122
AB WO 9309802 A UPAB: 931115
CNS injury in mammals is treated by admin., to the CNS, of transforming growth factor -beta1 (I), or its biologically active analogues.

(I) is given within 100 (pref. within 8) hr. of the injury occurring and the dose is 0.0001-100 micro-g per 100g body wt. Partic. (I) is delivered through a surgically inserted shunt into the cerebro-ventricle or peripherally for passage into the lateral ventricle of the brain. Suitable (I) analogues are the beta2; beta1,2; beta3; beta3,4; beta4 and beta5 forms of TGF.

Pref. (I) can be admin. together with other active agents, eg., growth factors to ameliorate loss of CNS cell, typically **insulin-like growth** factor.

USE/ADVANTAGE - Used to treat or prevent hypoxic, **ischaemic** or traumatic injury (typically in cases of perinatal asphyxia or stroke, or as a preventative before cardiac bypass surgery) or injuries caused by Parkinson's disease, multiple sclerosis or a demyelinising disorder. The injury may affect

non-cholinergic or glial cells.
Dwg.0/3

L75 ANSWER 7 OF 41 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 93-196731 [24] WPIDS
DNC C93-087150
TI Use of PDGF, preferably in combination with IGF-I - for promoting nerve growth in the treatment of multiple sclerosis, cerebral ischaemia, trauma etc..
DC B04
IN ANTONIADES, H N; HANSSON, H; LYNCH, S E
PA (MOLE-N) INST MOLECULAR BIOLOGY INC
CYC 38
PI WO 9310806 A1 930610 (9324)* EN 23 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA SE
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK LU MG MN MW NL NO PL RO RU SD SE UA
AU 9230668 A 930628 (9342)
EP 615452 A1 940921 (9436) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE
CH 684573 A5 941031 (9442)
JP 07501340 W 950209 (9515)
ADT WO 9310806 A1 WO 92-US9545 921104; AU 9230668 A AU 92-30668 921104; EP 615452 A1 EP 92-924312 921104, WO 92-US9545 921104; CH 684573 A5 WO 92-US9545 921104, CH 93-2309 921104; JP 07501340 W WO 92-US9545 921104, JP 93-510115 921104
FDT AU 9230668 A Based on WO 9310806; EP 615452 A1 Based on WO 9310806; CH 684573 A5 Based on WO 9310806; JP 07501340 W Based on WO 9310806
PRAI US 91-797315 911125
AB WO 9310806 A UPAB: 931116
Use of purified platelet-derived growth factor (PDGF) in the mfr. of a medicament for promoting growth of a mammalian nerve. The medicament may also include a second nerve growth promoting factor, e.g. **insulin-like growth** factor (IGF)-I, IGF-II or IGF-III.
USE/ADVANTAGE - The PDGF can promote growth of mammalian nerves in vivo. A combination of PDGF and IGF-I can provide a synergistic action in stimulating the in vivo regeneration of injured peripheral nerves. The action of PDGF and IGF-I results in axonal growth, proliferation of Schwann cells and myelin sheath formation. Used for treating diseases such as multiple sclerosis, amyotrophic lateral schlerosis or other neurodegenerative diseases resulting in damage to or atropy of nerve processes. They can also be used to regenerate nerves damaged due to trauma and to treat CNS disorders, e.g. **ischaemia** or tumours.
Dwg.0/1

L75 ANSWER 8 OF 41 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 94-006707 [01] WPIDS
DNC C94-002627
TI Prophylaxis of acute renal damage or failure in mammals - by administration of insulin-like growth factor I at the time of renal damage occurring.
DC B04
IN CLARK, R G
PA (GETH) GENENTECH INC
CYC 22

LTD

ing

US 5273961 A 931228 (9401)* 38 pp
WO 9406461 A1 940331 (9414) EN 56 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP NZ
AU 9349246 A 940412 (9431)
EP 661994 A1 950712 (9532) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
ADT US 5273961 A US 92-949594 920922; WO 9406461 A1 WO 93-US8734 930915;
AU 9349246 A AU 93-49246 930915; EP 661994 A1 EP 93-921612 930915,
WO 93-US8734 930915
FDT AU 9349246 A Based on WO 9406461; EP 661994 A1 Based on WO 9406461
PRAI US 92-949594 920922
AB US 5273961 A UPAB: 940217
Method comprises initiating administration to the mammal of an effective amt. of **insulin-like growth** factor I (IGF-I) before or at the time of **insulin-like growth** factor I (IGF-I) before or at the time that acute renal damage is expected to occur or is occurring, but not initiating administration after acute renal damage is expected to occur or has occurred.

USE - The method is used for the prophylactic treatment of patients at risk of acute renal damage or failure. The acute renal failure may be due to nephrotoxic damage or **ischemic** renal injury (claimed). The patient may be undergoing cardiac surgery or renal transplantation (claimed). The pref. dose of IGF-I is 0.01-1 mg/kg/day.
Dwg.0/21

L75 ANSWER 9 OF 41 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 95-147430 [19] WPIDS
DNN N95-115692 DNC C95-068450
TI New insulin secreting beta cell line for use in transplants - to control diabetes has inhibited insulin like growth factor 2 gene to prevent proliferation.
DC B04 D16 P32
IN ASFARI, M; DOCTEUR, C P; CZERNICHOW, P
PA (ASFA-I) ASFARI M
CYC 26
PI WO 9509231 A1 950406 (9519)* FR 18 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU BR CA CN FI HU JP KR NO US
FR 2710654 A1 950407 (9519) 13 pp
AU 9478157 A 950418 (9531)
ADT WO 9509231 A1 WO 94-FR1129 940927; FR 2710654 A1 FR 93-11687 930930;
AU 9478157 A AU 94-78157 940927
FDT AU 9478157 A Based on WO 9509231
PRAI FR 93-11687 930930
AB WO 9509231 A UPAB: 950524
Highly differentiated, insulin-secreting beta-cell line (INS-1) in which the expression characteristics are very close to those of normal beta cells and in which the gene for **insulin-like growth** factor II (IGF-II) is inhibited at least predominantly and permanently, is new. Also claimed are transplants for subcutaneous or intraperitoneal use contg. agglomerated 'pseudo-islets' incorporated into acrylic **tubular** membranes permeable to cpds. of mol. wt. < 50-80 kD and then distributed in the form of fibres.

USE - The new cells are used in transplants for physiologic control of glycaemia in subjects with insulin-dependent diabetes. 50-200multiplied by103 pseudo-islets are transplanted into an insulin-deficient subject.

ADVANTAGE - The cells have high insulin content, are sensitive to glucose, can express glucokinase and the Glut 2 glucose transporter, but are non-proliferative because of the defective IGF-II gene. Encapsulation of the cells avoids problems of immunological intolerance.

Dwg.0/0

L75 ANSWER 10 OF 41 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 95-206690 [27] WPIDS
DNC C95-095756
TI New treatment of renal disease using insulin-like growth factor complex - with insulin-like growth factor binding protein, for treating glomerulonephritis and diabetic or autoimmune nephropathy.
DC B04 C03
IN HIGLEY, H R; MAACK, C A
PA (CELT-N) CELTRIX PHARM INC
CYC 19
PI WO 9513824 A1 950526 (9527)* EN 24 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9510982 A 950606 (9538)
ADT WO 9513824 A1 WO 94-US13178 941115; AU 9510982 A AU 95-10982 941115
FDT AU 9510982 A Based on WO 9513824
PRAI US 93-152862 931115
AB WO 9513824 A UPAB: 950712

A method of treating renal disorders such as acute and chronic renal failure is new, by administering **insulin-like growth** factor (IGF-I) and IGF binding protein (IGFBP-3).

USE - Treatment with the IGF-I/IGFBP-3 complex increases renal **tubular** mass and potentiates and/or stimulates kidney function in affected patients. Humans, mammalian farm animals, sport animals and pets may be treated. The complex can treat disorders such as glomerulonephritis, glomerulosclerosis, interstitial nephritis, acute **tubular** necrosis due to **ischaemia** or drug-induced toxicity, diabetic nephropathy or autoimmune nephropathy.

Dwg.0/1

L75 ANSWER 11 OF 41 CAPLUS COPYRIGHT 1996 ACS
AN 1989:109023 CAPLUS
DN 110:109023
TI Induction of insulin-like growth factor I messenger ribonucleic acid during regeneration of rat skeletal muscle
AU Edwall, D.; Schalling, M.; Jennische, E.; Norstedt, G.
CS Karolinska Inst., Huddinge Univ. Hosp., Huddinge, S 141 82, Swed.
SO Endocrinology (Baltimore) (1989), 124(2), 820-5
CODEN: ENDOAO; ISSN: 0013-7227
DT Journal
LA English
AB After irreversible damage to muscle cells was induced in the extensor digitorum longus muscle of adult rats by **ischemia**, preceded by glycogen depletion, increased **insulin-like** growth factor-I (**IGF**-1) mRNA levels were

demonstrated within 24 h after injury; max. levels were achieved in 3 days and **decreased** to approx. normal levels by 10 days. Changes in **IGF**-I mRNA levels were not seen in undamaged contralateral extensor digitorum longus muscles during the exptl. period. An increase in **IGF**-I mRNA was also evident in injured muscles of hypophysectomized animals. In situ hybridization at the time of max. induction showed the presence of **IGF**-I mRNA in proliferating myoblasts and in satellite cells. **IGF**-I, thus, may act as a locally produced non-growth hormone dependent trophic factor during regeneration of skeletal muscle after injury.

L75 ANSWER 12 OF 41 MEDLINE
AN 93101629 MEDLINE
TI Insulin-like growth factor I accelerates recovery from ischemic acute tubular necrosis in the rat.
AU Miller S B; Martin D R; Kissane J; Hammerman M R
CS Department of Internal Medicine, George M. O'Brien Kidney and Urological Diseases Center, Washington University School of Medicine, St. Louis, MO 63110.
NC DK-27600 (NIDDK)
DK-42958 (NIDDK)
DK-45181 (NIDDK)
+
SO Proc Natl Acad Sci U S A, (1992 Dec 15) 89 (24) 11876-80.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9303
AB The effects of administering insulin-like growth factor I (IGF-I) were examined in a model of ischemic acute tubular necrosis in rats. Injury was induced by 75 min of bilateral renal artery occlusion. Compared to rats administered vehicle, rats administered IGF-I (100 micrograms/day via continuous subcutaneous infusion) had significantly lower serum creatinine and blood urea nitrogen levels over the course of 7 days postocclusion. Glomerular filtration rate as determined by inulin clearance was examined on day 2 postocclusion and was significantly increased in IGF-I-treated animals (0.16 +/- 0.02 ml per min per 100 g of body weight) compared to vehicle-treated controls (0.08 +/- 0.02 ml per min per 100 g of body weight). The weight loss that occurred during the course of acute tubular necrosis was ameliorated by IGF-I. Mortality was reduced from 36.7% in vehicle-treated rats to 7.1% in rats administered IGF-I. Histologically, there was much less renal injury evident at day 7 postocclusion in the IGF-I-treated rats compared to vehicle-treated controls. In contrast, growth hormone (200 micrograms administered subcutaneously for 4 days) did not affect recovery of renal function or reduce mortality postreperfusion. This report demonstrates a beneficial effect of IGF-I administration in the setting of acute tubular necrosis. Several properties of IGF-I render it a pharmacological agent with excellent potential for treatment of this condition in humans.

L75 ANSWER 13 OF 41 MEDLINE
AN 92134275 MEDLINE
TI A role for IGF-1 in the rescue of CNS neurons following

hypoxic-ischemic injury.
AU Gluckman P; Klempt N; Guan J; Mallard C; Sirimanne E; Dragunow M; Klempt M; Singh K; Williams C; Nikolics K
CS Department of Paediatrics, University of Auckland, New Zealand.
SO Biochem Biophys Res Commun, (1992 Jan 31) 182 (2) 593-9.
Journal code: 9Y8. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9205
AB Three days after unilateral hypoxic-ischemic injury in infant rats insulin-like growth factor 1 (IGF-1) production by astrocytes was enhanced in the injured region. This was associated with increased expression of mRNA for IGF binding protein-3 but not for binding protein-1. In adult rats a single lateral cerebroventricular injection of IGF-1 two hours following a similar injury markedly reduced neuronal loss. It is suggested that endogenous IGF-1 is neurotrophic and that centrally administered IGF-1 may have therapeutic potential for brain injury.

L75 ANSWER 14 OF 41 MEDLINE
AN 94154412 MEDLINE
TI Insulin-like growth factor 1 and recovery from experimental acute renal failure [editorial; comment].
CM Comment on: Nutrition 1993 Nov-Dec;9(6):528-31
AU Hirschberg R
SO Nutrition, (1993 Nov-Dec) 9 (6) 562-3.
Journal code: BEU. ISSN: 0899-9007.
CY United States
DT Commentary
Editorial
LA English
FS Priority Journals
EM 9406

L75 ANSWER 15 OF 41 MEDLINE
AN 94154402 MEDLINE
TI Insulin-like growth factor 1 and endotoxin-mediated kidney dysfunction in critically ill, parenterally fed rats [see comments].
CM Comment in: Nutrition 1993 Nov-Dec;9(6):562-3
AU Manzo C B; Dickerson R N; Settle R G; Rajter J J
CS University of Tennessee, Memphis 38163.
NC 1R15DK46545-01 (NIDDK)
SO Nutrition, (1993 Nov-Dec) 9 (6) 528-31.
Journal code: BEU. ISSN: 0899-9007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9406
AB Endotoxemia is an important contributor to the pathogenesis of acute kidney failure in sepsis. Data suggest insulin-like growth factor 1 (IGF-1) can increase creatinine clearance in healthy humans. The influence of recombinant human IGF-1 on kidney function in endotoxemia was investigated in 34 male Sprague-Dawley rats. After venous cannulation and postoperative parenteral nutrition (PN), the

Animals were randomly assigned to receive PN only, PN plus Escherichia coli lipopolysaccharide (LPS), or PN plus LPS plus IGF-1. Urine output was significantly higher for the IGF-1 and control groups compared with the LPS group (18.9 +/- 5.7, 13.0 +/- 3.8, and 17.7 +/- 3.1 ml/day for control, LPS, and IGF-1 groups, respectively, analysis of variance, $p < 0.05$). Creatinine clearance was significantly higher in the IGF-1 group than the LPS group and exceeded the control group (0.49 +/- 0.27, 0.36 +/- 0.14, and 0.65 +/- 0.27 ml.min-1.100(-1) g body wt) for control, LPS, and IGF-1, respectively (analysis of variance, $p < 0.05$). IGF-1 ameliorates the effects of endotoxin on kidney function as measured by creatinine clearance and urine output in endotoxemic parenterally fed rats.

L75 ANSWER 16 OF 41 MEDLINE
AN 94066033 MEDLINE
TI Insulin-like growth factor-I ameliorates transient ischemia-induced acute renal failure in rats.
AU Noguchi S; Kashihara Y; Ikegami Y; Morimoto K; Miyamoto M; Nakao K
CS Preclinical Research Department, CIBA-GEIGY Japan, Limited, Hyogo.
SO J Pharmacol Exp Ther, (1993 Nov) 267 (2) 919-26.
Journal code: JP3. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9403
AB Acute renal failure in rats was induced by transient occlusion of bilateral renal arteries and veins to investigate whether insulin-like growth factor-I (IGF-I) has an effect on the damaged renal function or not. Administration of IGF-I at 0.01, 0.1 and 1 mg/kg by s.c. injection caused a 18.7, 33.0 and 66.5% increase of glomerular filtration rate and 54.8, 61.2 and 84.1% decrease of blood urea nitrogen, respectively, compared with the values in the saline-treated group 2 days after ischemia. Other renal parameters tested such as fractional excretion of sodium, N-acetyl-beta-D-glucosaminidase and tubular reabsorptance of phosphorus which are thought to represent renal function of proximal and distal tubules, respectively, were also improved by IGF-I treatment. A histochemical study also supported these observations. Severe epithelial necrosis of proximal tubules and decrease of brush borders were observed 2 days after transient ischemia in the saline-treated group, whereas marked histochemical alterations were not observed in the IGF-I-treated group. L-NG-nitroarginine, an inhibitor of nitric oxide synthetase, prevented the improvement of glomerular filtration rate and blood urea nitrogen by IGF-I at 1 mg/kg, suggesting that the ameliorative action on renal function by IGF-I is mediated via nitric oxide, possibly its vasodilating action. These findings provide the first evidence for the efficacy of IGF-I in the model of acute renal failure, suggesting that IGF-I may be useful for the treatment of acute renal failure.

L75 ANSWER 17 OF 41 MEDLINE
AN 93366962 MEDLINE
TI Changes in insulin-like growth factor 1 receptor density after transient cerebral ischemia in the rat. Lack of protection against ischemic brain damage following injection of insulin-like growth factor 1.

AU Bergstedt K; Wieloch T
CS Laboratory for Experimental Brain Research, Lund University, Lund Hospital, Sweden.
SO J Cereb Blood Flow Metab, (1993 Sep) 13 (5) 895-8.
Journal code: HNL. ISSN: 0271-678X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9312
AB Binding of 125I-insulin-like growth factor-1 (125I-IGF-1) to rat brain slices was studied after 15 min of two-vessel occlusion ischemia and 1 h to 4 days of recirculation. Ligand binding in the hippocampus increased at 6 h post ischemia in the CA1 and CA3 regions and the dentate gyrus, suggesting that the IGF-1 receptors were up-regulated, while no change was seen in neocortex and striatum. Intracerebroventricular injections of IGF-1 (2 micrograms) prior to and after transient cerebral ischemia did not reduce neuronal damage. The increased up-regulation on IGF-1 receptors and the absence of neuroprotection by IGF-1 suggest that the intracellular signal transduction chain activated by the IGF-1 receptor may be interrupted.

L75 ANSWER 18 OF 41 MEDLINE
AN 93301012 MEDLINE
TI The effects of IGF-1 treatment after hypoxic-ischemic brain injury in adult rats.
AU Guan J; Williams C; Gunning M; Mallard C; Gluckman P
CS Department of Paediatrics, University of Auckland, New Zealand.
SO J Cereb Blood Flow Metab, (1993 Jul) 13 (4) 609-16.
Journal code: HNL. ISSN: 0271-678X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9309
AB Intraventricular injection of insulin-like growth factor 1 (IGF-1) 2 h after hypoxic-ischemic injury reduces neuronal loss. To clarify the mode of action, we compared histological outcome between treatment groups in the following three studies: 0, 0.5, 5, and 50 micrograms IGF-1 given 2 h after injury; 0 and 20 micrograms IGF-1 given 1 h before; and 20 micrograms IGF-1 and insulin or vehicle alone given 2 h after. Unilateral hypoxic-ischemic injury was induced in adult rats by ligation of the right carotid and exposure to 6% O2 for 10 min. Histological outcome was evaluated in the cortex, striatum, and hippocampus 5 days later. Five to 50 micrograms IGF-1 reduced the incidence of infarction and neuronal loss in a dose-dependent manner in all regions ($p < 0.05$), and 50 micrograms reduced the infarction rate from 87 to 26% ($p < 0.01$). Pretreatment did not alter outcome. IGF-1 improved outcome compared with equimolar doses of insulin ($p < 0.05$) and did not affect systemic glucose concentrations or cortical temperature. The results indicate that the neuronal protective effects of IGF-1 are specific and are not mediated via insulin receptors, hypothermia, or hypoglycemic mechanisms. Centrally administered IGF-1 appears to provide worthwhile trophic support to cells within most cerebral structures after transient hypoxic-ischemic injury.

ANSWER 19 OF 41 MEDLINE
93253077 MEDLINE
Recombinant human insulin-like growth factor-I accelerates recovery and reduces catabolism in rats with ischemic acute renal failure.
Ding H; Kopple J D; Cohen A; Hirschberg R
Division of Nephrology and Hypertension, Harbor-UCLA Medical Center, Torrance 90509.
SO J Clin Invest, (1993 May) 91 (5) 2281-7.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9308
AB This study evaluated whether recombinant human insulin-like growth factor-I (rhIGF-I) enhances recovery of renal function and reduces catabolism in rats with ischemic acute renal failure (ARF). ARF and sham rats received subcutaneous injections of either rhIGF-I or vehicle three times daily starting 5 h after surgery. Serum creatinine and urea, which initially rose similarly in the ARF+vehicle and ARF+rhIGF-I rats, increased more slowly after commencing the rhIGF-I injections. 72 h after surgery, the ARF+rhIGF-I rats, in comparison with ARF+vehicle animals, showed significantly greater renal plasma flow and filtration fraction, a fivefold higher glomerular filtration rate, greater renal cortical IGF-I levels, increased proliferating cell nuclear antigen expression in proximal tubule nuclei and enhanced DNA synthesis in the renal cortex, corticomedullary junction, glomeruli, and tubules as demonstrated by [3H]thymidine incorporation and in corticomedullary junction tubules as determined by autoradiography. Estimated total nitrogen output (ETNO) was greater in ARF+vehicle than in ARF+rhIGF-I or sham rats throughout the study. ETNO in ARF+rhIGF-I rats returned to sham values by the second day after surgery. 72 h after surgery, protein degradation was increased and protein synthesis reduced in the epitrochlearis muscle of ARF+vehicle as compared with ARF+rhIGF-I or sham+vehicle rats. Thus, treatment with rhIGF-I starting 5 h after inducing ischemic ARF in rats increases recovery of renal function, enhances formation of new renal tubular cells, lowers protein degradation, and increases protein synthesis in skeletal muscle and reduces net catabolism.

L75 ANSWER 20 OF 41 BIOSIS COPYRIGHT 1996 BIOSIS
AN 93:324279 BIOSIS
DN BA96:32629
TI EFFECTS OF IGF-I ON RENAL FUNCTION IN PATIENTS WITH CHRONIC RENAL FAILURE.
AU O'SHEA M H; MILLER S B; HAMMERMAN M R
CS RENAL DIV., BOX 8126, DEP. INTERNAL MED., WASHINGTON UNIV. SCH. MED., 660 SOUTH EUCLID AVE., ST. LOUIS, MO 63110, USA.
SO AM J PHYSIOL 264 (5 PART 2). 1993. F917-F922. CODEN: AJPHAP ISSN: 0002-9513
LA English
AB **Insulin-like growth** factor I (IGF-I) has been shown to increase glomerular filtration rate and renal plasma flow in rats and humans with normal renal function. However, rats with reduced renal function are resistant to these effects. To